# COVID-19 Associated Pulmonary Aspergillosis at a Hospital in Nicaragua: Prevalence and Risk Factors for Mortality.

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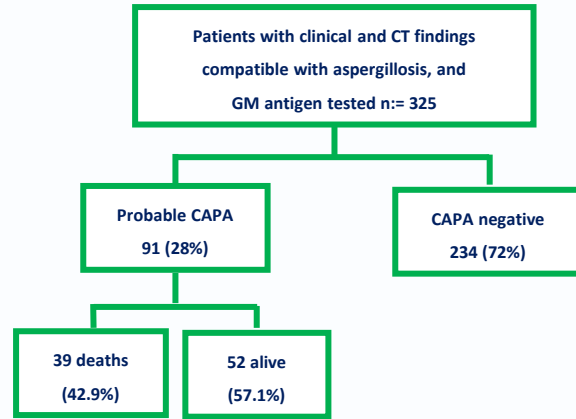Hospital Dr. Fernando Vélez Paiz.  Managua, Nicaragua.

**Background:** COVID-19 associated pulmonary aspergillosis (CAPA) is a newly recognized clinical entity.  Alterations in the mucociliary clearance ability, epithelial damage, lymphopenia, and the use of steroids and monoclonal antibodies could be contributing factors for the development of CAPA.

**Objective:** The aim of this study was to determine the prevalence of probable CAPA, risk factors and clinical outcomes in patients with COVID-19 admitted in one of the main hospitals in Nicaragua.

**Methods:** This is a retrospective cohort study of patients admitted with the diagnosis of COVID-19 in the Hospital Dr. Fernando Vélez Paiz of Managua, Nicaragua.  The criteria of probable CAPA was established using the criteria of ECMM/ISHAM consensus.  Serum *Aspergillus* galactomannan antigen (GM) lateral flow assay (IMMY) was determined in patients with suspect of CAPA (clinical and CT findings compatible with aspergillosis).  An optical index > 0.5 was considered positive.  Different clinical and laboratory variables, and clinical outcomes were evaluated.

**Results:** A total of 325 patients were included in the study.  Ninety-one patients were diagnosed with probable CAPA (prevalence of 28%), with a mortality rate of 42.9% (Figure 1).  The prevalence of CAPA was comparable with the study of Bartoletti in Italy (Table 1).   The mean age was 56.6 ± 15.0 years old.   The most important comorbidities were hypertension (44.2%), diabetes mellitus (29.4%), and COPD (14.8%).  Forty-two of the survivors had a chronic medical condition vs 39 in the non-survivors (Table 2).  Lymphopenia was a remarkable finding (56% of the patients) and was present in 76.9% of the non-survivors (Figure 2).  The most frequent radiological pattern in the chest CT were:  "crazy paving" (56%), ground glass opacities (28.5%), and diffuse reticulonodular (10.9%) (Table 3). The risk factors associated with mortality in the patients with CAPA were: need of admission to Intensive Care Unit (ICU) (OR: 17.3; 95% CI: 3.6-81.9), any chronic medical condition (OR: 9.28; 95% CI: 1.13-75.90), COPD (OR: 6.41; 95% CI: 1.64-24.90), use of steroids (OR: 5.03, 95% CI: 1.55-16.30), lymphopenia < 1,500 cells/mL (OR: 4.92; 95% CI: 1.94-12.40), "crazy paving" pattern in CT (OR: 4.92; 95% CI: 1.94-12.40), and diabetes mellitus (OR: 3.60, 95% CI: 1.41-9.15) (Table 4).



Figure 1.-  Flowchart and prevalence of COVID-19 Associated Pulmonary Aspergillosis (CAPA)

| Comorbidities | CAPA Survivors n= 52 (%) | CAPA Non-Survivors n= 39 (%) | p |
|---|---|---|---|
| Any comorbidity | 42 (80.7) | 39 (100.0) | 0.003 |
| Diabetes mellitus | 10 (19.2) | 18 (46.1) | 0.006 |
| COPD | 3 (5.7) | 11 (28.2) | 0.006 |
| Hypertension | 24 (46.1) | 18 (46.1) | 1 |
| Cancer | 0 | 5 (12.8) | 0.02 |
| Pulmonary Tuberculosis | 1 (1.9) | 5 (12.8) | 003 |

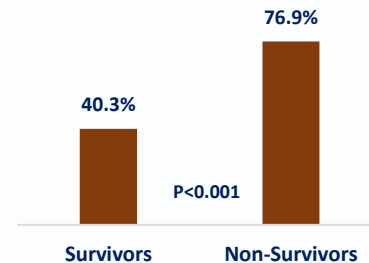Table 2.-  Comorbidity and mortalitiy in patients with CAPA

| Study | Prevalence of CAPA Cases/N (%) | Mortality CAPA |
|---|---|---|
| Sivasubramanian et al (2021) - USA | 48/970 (4.9%) | 83% |
| Janssen et al. (2021) - Netherlands | 68/823 (7.6%) | 49.2% |
| Rouze et al. (2022) - France | 31/568 (5.4%) | 35.7% |
| Gangneux et al. (2021) - France | 76/509 (14.9%) | 61.8% |
| Permpalung et al. (2021) - USA | 39/396 (9.8%) | 56% |
| Xu et al. (2021) - China | 78/335 (23.3%) | 52.6% |
| López A. (this study) - Nicaragua | 91/325 (28.0%) | 42.9% |
| Machado et al. (2020) - Spain | 6/239 (2.5%) | 100% |
| Roman – Montes et al. (2020) - Mexico | 14/144 (9.7%) | 57.1% |
| Bartoletti et al. (2020) - Italy | 30/108 (27.7%) | 44% |

Table 1.-  Comparison of prevalence and mortality of different studies about CAPA



Figure 2.-  Patients with lymphopenia <1,500 cells/mm³ in survivors and non-survivors with CAPA

| Chest CT Pattern | CAPA Survivors n= 52 (%) | CAPA Non-Survivors n= 39 (%) | p |
|---|---|---|---|
| Crazy paving | 21 (40.39) | 30 (76.9) | <0.001 |
| Groud glass opacities | 19 (36.5) | 7 (17.9) | 0.05 |
| Reticulonodular | 8 (15.39) | 2 (5.1) | 0.12 |
| Others | 1 (3.8) | 2 (5.1) | 0.76 |

Table 3.-  Patterns in the chest CT-Scan and mortality in patients with CAPA

| Risk factors for mortality in CAPA | OR (95% CI) |
|---|---|
| Need of admission to ICU | 17.30 (3.60-81.90) |
| Any chronic medical condition | 9.28 (1.13-75.90) |
| COPD | 6.41 (1.64-24.90) |
| Treatment with steroids for the COVID-19 | 5.03 (1.55-16.30) |
| Crazy paving in the chest CT | 4.92 (1.94-12.40) |
| Diabetes mellitus | 3.60 (1.41-9.15) |

Table 4.-  Risk factors for mortality in patients with CAPA

**Conclusion:** The prevalence of probable CAPA in this study is relatively high.  The mortality was of 42.9%.  Risk factors for mortality were admission to ICU, chronic medical conditions (COPD and diabetes mellitus), use of steroids, lymphopenia, and radiological "crazy paving" pattern.

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